UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/719,909 | 03/01/2001 | Thomas William Rademacher | 1012-102US | 6839 |

7590 04/09/2003

Jonathan Alan Quine
Law Offices of Jonathan Alan Quine
PO Box 458
Alameda, CA 94501

| EXAMINER | |
|---|---|
| YOUNG, JOSEPHINE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | 12 |

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/719,909 | RADEMACHER ET AL. | |
| | Examiner | Art Unit | |
| | Josephine Young | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *8-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7, 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of Group I in Paper No. 11, mailed January 17, 2003, is acknowledged. The traversal is on the ground(s) that the newly amended claims are now linked by a special technical feature, namely compositions comprising an inositolphosphoglycan (IPG) and ribose. This is not found persuasive because the inventions still do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. As set forth herein, compositions comprising IPG and ribose lack an inventive step. Therefore, the technical feature linking the inventions and does not define a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 8-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

### *Specification*

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 7 is directed to a composition in powder or concentrate form that can be used to prepare a liquid composition. However, the specification, on page 13, lines 27-31, only teaches compositions that may be supplied in the form of a powder or concentrate from

which a composition can be prepared, and does not specifically disclose that the powder or concentrate form can be used to prepare a liquid composition, in particular.

### *Claim Rejections - 35 USC § 112, First Paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below in In re Wands USPQ2d 14000. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention.

These factors include

(1) quantity of experimentation necessary,

(2) the amount of guidance presented,

(3) the presence or absence of working examples,

(4) the nature of the invention,

(5) the state of the prior art,

(6) the predictability of the art and

(7) the breath of the claims.

Claims 1 and 4-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using compositions comprising IPG type P, does not reasonably provide enablement for making and using compositions comprising IPG type A. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

With regard to factors (1) and (2) cited above, undue experimentation is required to determine if IPG type A would sufficiently stimulate pyruvate dehydrogenase phosphatase to be useful in compositions of the disclosed utility, namely, for treating or preventing ischaemic reperfusion injury, preserving an organ for transplantation or reducing loss of cellular ATP. There has not been provided adequate guidance in the written description for accomplishing such, as only methods comprising stimulation of pyruvate dehydrogenase phosphatase by IPG type P were discussed.

With regard to factors (4), (5) and (6), it is noted that there is a great deal of unpredictability in the art. For example, IPG type A is not known for its ability to stimulate pyruvate dehydrogenase phosphatase. Further, type A mediators are primarily known for their ability to mimic the lipogenic activity of insulin on adipocytes. See for example CARO et al., Biochemical and Molecular Medicine, **1997**, *61*, 214-228 (AF: PTO/SB/08A-B mailed July 13, 2001). The art at the time the invention was made fails to establish predictability with regard to the properties of IPG type A needed to use the compositions as instantly claimed.

With regard to factors (3) and (7), it is noted that while there are some working examples of compositions comprising IPG type P, it is not seen as sufficient to support the breath of the

claims. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. See In re Gardner et al. 166 USPQ 138 (CCPA 1970).

***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "IPG synthetic analogue" in claim 1 renders the claims in which it appears indefinite. In the absence of the specific modification to IPG or distinct language to describe the structural modifications or the chemical names of the IPG synthetic analogue of this invention, the identity of said IPG synthetic analogue would be difficult to describe and the metes and bounds of said compositions comprising a IPG synthetic analogue that Applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

Similarly, the term "nucleotide precursor" in claim 4 renders the claims in which it appears indefinite. In the absence of the specific modifications to the nucleotide or distinct language to describe the structural modifications or the chemical names of the nucleotide precursor of this invention, the identity of said nucleotide precursor would be difficult to describe and the metes and bounds of said compositions comprising a nucleotide precursor that

Applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over the articles ZIMMER et al., Molecular and Cellular Biochemistry, **1996**, *106/161*, 101-109 (BD: PTO/SB/08A-B mailed July 13, 2001) and STANLEY et al., Cardiovascular Research, 1997, 33, 243-257 (AX: PTO/SB/08A-B mailed July 13, 2001) and International Patent Publication WO 98/11435 to HOEFT RADEMACHER LIMITED (N: PTO-892 mailed November 25, 2002).

Applicant claims compositions comprising inositolphosphoglycan (IPG), and in particular P-type IPG, or its synthetic analogue, in combination with ribose. Further, Applicant

claims compositions comprising adenosine, purine or a nucleotide precursor. Finally, Applicant claims various pharmaceutical formulations.

ZIMMER discloses that after reperfusion, repletion of the ATP pool is only attained via the very slow de novo synthesis of adenine nucleotides, since the precursor substrate for the synthesis of purine and pyrimidine nucleotides, 5-phosphoribosylpyrophosphate (PRPP), is generated in the oxidative pentose phosphate pathway (PPP) and very limited in the heart. Further, ZIMMER teaches that oxidative PPP is the link between carbohydrate and fatty acid as well as purine and pyrimidine nucleoside metabolism. See page 101, right column. ZIMMER teaches on page 106, right column, first and second paragraph under the heading Ribose, that ribose leads to the enhancement of adenine nucleotide biosynthesis by either attenuating or preventing the decline of the myocardial ATP pool. Finally, ZIMMER teaches on page 107, right column, first full paragraph, that ribose can be combined with other drugs that are used in conventional therapy of heart disease. In particular, on page 107, right column, second full paragraph, ZIMMER teaches that when ribose was given in combination with adenine or inosine, cardiac ATP levels returned to normal following reduction of the cardiac ATP pools using iso-proterenol.

ZIMMER does not explicitly state that ribose can be combined with a compound that activates PDH via stimulation of PDH phosphatase, such as IPG, or type-P IPG in particular. Further, ZIMMER does not disclose any particular pharmaceutical formulation.

STANLEY teaches that myocardial ischaemia results from a fall in glycogen concentration. See page 244, right column, last sentence of the first paragraph, as well as Sections 4 and 5. Further, STANLEY teaches on page 245, left column, first full paragraph, that

glycolytically derived ATP is essential for optimal diastolic relaxation. On page 249, right column, first full paragraph, STANLEY teaches that metabolic therapies for the treatment of heart disease have focused on (1) increasing myocardial glycolysis by increasing glucose uptake during ischaemia or by increasing glycogen levels prior to a surgical procedure; (2) inhibiting myocardial fatty acid oxidation, thus increasing carbohydrate oxidation and flux through pyruvate dehydrogenase (PDH); or (3) activating PDH (for example by stimulating PDH phosphatase) and increasing carbohydrate oxidation. Finally, STANLEY teaches on page 253, in the Summary and Conclusions, that metabolic interventions aimed at enhancing glucose utilization and pyruvate oxidation at the expense of fatty acid oxidation is a valid therapeutic approach to the treatment of myocardial ischaemia.

HOEFT RADEMACHER teaches that IPG P-type activates pyruvate dehydrogenase phosphatase. See page 2, lines 26-34. Further, HOEFT RADEMACHER discloses on pages 20-21, various pharmaceutical formulations comprising IPG mediators, including pharmaceutical compositions in powder or liquid form, optionally including an excipient.

It would have been obvious to one of ordinary skill in the art to make and use compositions comprising type P IPG and ribose, optionally in combination with adenosine or inosine, for the treatment of various forms of heart disease, as ZIMMER teaches that ribose can be combined with other drugs that are used in conventional therapy of heart disease, including adenine or inosine, STANLEY discloses that one such conventional therapy is a metabolic therapy focused on activating PDH (for example by stimulating PDH phosphatase), and HOEFT RADEMACHER teaches that IPG P-type activates PDH phosphatase. A skilled artisan would have been motivated and have had a reasonable expectation of success to make and use such

compositions in the various disclosed pharmaceutical formulations, as such formulations are well within the purview of the prior art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

***Conclusion***

Claims 1-25 are pending. Claims 1-7 are rejected. Claims 8-25 are withdrawn. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Josephine Young whose telephone number is (703) 605-1201. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (703) 308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JY
April 7, 2003

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600